REMARKS

Claims 24-30 and 38-59 are pending in this application. Claims 24-30 and 38-59 were variously rejected under 35 U.S.C. §112, first paragraph. Claims 24 and 38-40 were variously rejected under 35 U.S.C. §102(e) or §103. Claims 24-30 and 38-59 were variously rejected under the judicially created doctrine of obviousness-type double patenting. Claim 24 and the specification were objected to.

By this amendment, claim 24 has been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendment can be found, *inter alia*, throughout the specification and the claims as originally filed. For example, support for the amendment can be found at page 13, second full paragraph, of the substitute specification. This amendment corrects the typographical error to the term "effective" in claim 24 and, thus, addresses the objection raised on page 20 of the Office Action. Applicants respectfully request entry of this amendment under 37 C.F.R. §1.116(b).

The amendment is made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover, have not acquiesced to any rejections or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Specification Objection

The 18 August 2003 Preliminary Amendment was objected to under 35 U.S.C. §132(a) as allegedly introducing new matter into the disclosure. The Examiner asserts that the filed amendment is deficient for not being accompanied by "a statement that the material being inserted is the material previously incorporated by reference AND that the amendment contains no new matter." Office Action, page 20. Accordingly, filed herewith is an affidavit, executed by Applicants' representative, stating that the new paragraphs submitted in the 18 August 2003

Preliminary Amendment consist solely of material incorporated by reference in the referencing application, WPI Acc. No. 93-182488/22 which corresponds to WO 93/10146. No new matter is included in these new paragraphs. Thus, withdrawal of this objection is respectfully requested.

The Substitute Specification submitted 10 May 2005, pursuant to 37 C.F.R. §1.125, includes the new paragraphs added in the 18 August 2003 Preliminary Amendment and, as stated upon its submission, contains no new matter. Applicants respectfully request entry of this Substitute Specification.

Finally, Applicants respectfully note that the same change to the specification was made in prior Application Serial No. 08/302,069, which issued as U.S. Pat. No. 6,114,304, and Application Serial No. 09/576,062, which issued as U.S. Patent No. 6,608,029.

Rejections under 35 U.S.C. §112, first paragraph

Claims 24-30 and 38-59 were variously rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description and enablement requirements.

New Matter

Claims 24-30 and 38-59 were rejected as allegedly failing to comply with the written description requirement regarding new matter. Applicants respectfully traverse this rejection.

On page 3 of the Office Action, the Examiner alleges that the presently claimed subgenus of amylin agonists of claims 25-30 and 41-59 are not described in the specification nor is there support for the scope of amino acids encompassed by the proviso "then one or more of any A1 to M1 is not an L-amino acid and Z is not amino." Applicants respectfully submit that the substitute specification (submitted 10 May 2005) describes amylin agonists as claimed, including those containing D-amino acids. See, for example, substitute specification at the paragraph bridging pages 16 and 17 and at page 18, fourth full paragraph. As discussed herein, this description was incorporated by reference in the originally filed specification. Thus, amylin agonists of claims 25-30 and 41-59 are described in the originally filed specification.

On page 21 of the Office Action, the Examiner states that support for the language "reduce or moderate" of claim 24 was not indicated. Applicants respectfully submit that the specification clearly describes the use of amylin or an amylin agonist to reduce or moderate a postprandial rise in plasma glucose. For example, at page 25 of the substitute specification,

results of studies are summarized in which administration of amylin or an amylin agonist results in a reduction of post-prandial glucose levels as well as the peak plasma glucose concentration of subjects. The subjects in the studies experienced a glucose smoothing effect and a plasma glucose plateau at a level lower that the control subjects[1], indicating a moderation in a postprandial rise in plasma glucose. Thus, the specification describes the use of amylin or an amylin agonist to reduce or moderate a postprandial rise in plasma glucose.

Accordingly, the pending claims are fully described in the specification as filed and Applicants respectfully request reconsideration and withdrawal of the new matter rejections.

Written Description

Claims 24 and 38-40 were rejected as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

As amended herein, the claimed invention is directed to a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administration of an amylin or an amylin agonist to the mammal, wherein the amylin agonist is a peptide. The specification lists many examples of peptidic amylin agonists for use in the claimed invention. See, for example, page 20 of the substitute specification. The specification provides physical and chemical characteristics, including receptor binding activity, of exemplary amylin agonist peptides.[2] The specification also provides functional characteristics of exemplary amylin agonist peptides such as moderating the postprandial rise in plasma glucose, reducing gastric motility, slowing gastric emptying, and demonstrating amylin activity in a soleus muscle assay.[3] Also, information regarding peptides and peptide structure in general was well known in the art at the time the application was filed. Further, information regarding peptidic amylin agonists specifically, including structural information, was known in the art at the time of filing. See, for example, the amylin agonists described in reference WPI Acc. No. 93-182488/22, cited and incorporated by reference in the specification. The specification in combination with that known

1 See, for example, pages 31 and 35 of the substitute specification.
2 See, for example, pages 42-50 of the substitute specification.
3 See, for example, pages 30-40 and 50-52 of the substitute specification.

in the art adequately describes possession of the claimed genus "amylin agonist peptide" to one skilled in the art.

Quoting from the Office's Written Description Requirement Guidelines, the court in *Enzo* stated that "the PTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, 66 Fed. Reg. At 1106 (emphasis added)." *Enzo Biochem, Inc. v Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002).

Applicants respectfully submit that the specification in combination with that known in the art provides a description of sufficient, relevant, identifying structural and functional characteristics of an amylin agonist peptide to adequately describe possession of the claimed genus to one skilled in the art. Thus, the pending claims are fully described in the specification as filed. Accordingly, Applicants respectfully submit that the written description requirement has been met.

Enablement

Claims 24 and 38-40 were rejected for allegedly not enabling any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Applicants respectfully traverse this rejection.

As amended herein, the claimed invention is directed to a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administration of an amylin or an amylin agonist to the mammal, wherein the amylin agonist is a peptide.

Applicants have provided direction and guidance, and have presented numerous examples of amylin agonist peptides such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation. For example, page 20 of the substitute specification provides over 25 examples of peptidic amylin agonists for use in the invention. Pages 23-25 and 42-49 of the substitute specification describe methods for making the disclosed and additional amylin agonist peptides. At pages 21-22, 30-40, and 49-52, the substitute specification provides methods by which the skilled artisan can assess the activity of any peptidic

amylin agonist. The specification provides guidance for determining amylin agonist activity in receptor binding assays, soleus muscle assays, gastric motility assays, and postprandial plasma glucose assays. Applicants also submit that peptidic amylin agonists were known in the art at the time the application was filed, as shown by reference WPI Acc. No. 93-182488/22 cited and incorporated by reference in the specification. Such extensive disclosure provides adequate guidance such that a skilled artisan would be able to practice the invention without undue experimentation.

The court in *In re Wands*, 858 F.2d 731,737 (Fed. Cir. 1988), found that the enablement requirement was satisfied by a "disclosure [that] provides considerable direction and guidance on how to practice [the] invention and presents working examples," in view of the fact that "[t]here was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *Id.* at 740. Fulfillment of the enablement requirement does not require that every embodiment of the invention be predictable. Rather, unpredictability is permitted, the level of unpredictability permitted depending on the level of guidance provided by the specification and the knowledge in the art. Applicants respectfully note that the test for enablement is not whether the amount of experimentation is required to practice the invention, but rather whether the amount of experimentation is "undue." *Id.* at 731,737. Applicants respectfully submit that the specification has provided adequate guidance to the skilled artisan with respect to making and using amylin agonist peptides and that the skilled artisan would be able to extend the teachings of the specification and the art to the methods as claimed.

Also, in order to make this rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993): M.P.E.P. §2164.04. Applicants respectfully submit that the Examiner has not provided acceptable documentation or sound scientific reasoning to support any doubt of the teachings of the specification. Unless such documentation and/or scientific reasoning are adduced, the statements made in the specification are to be taken at face value.

Thus, Applicants respectfully submit that a *prima facie* case of lack of enablement has not been established and the pending claims are in compliance with the enablement requirements.

In sum, Applicants submit that the pending claims fall within the subject matter that is described and enabled by the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. 112, first paragraph.

Rejections under 35 U.S.C. §102/103

Claims 24 and 38 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by Liu et al. (U.S. Pat. No. 6,136,820; "Liu"). Claims 24 and 38-40 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by Liu or alternatively rejected under 35 U.S.C. §103 as allegedly obvious over Liu in view of Meezan et al. (U.S. Pat. No. 5,817,634; "Meezan"). Applicants respectfully traverse these rejections.

As amended, claim 24 is directed to a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administration of an amylin or an amylin agonist to the mammal, wherein the amylin agonist is a peptide. Claim 38 is directed to the method of claim 24 wherein the mammal has diabetes.

Liu describes treating diabetes and postprandial hyperglycemia in diabetic individuals through administration of castanospermine, an alkaloid. See, for example, Liu, col. 1, lines 15-29, and claims 1-2. Liu does not teach administration of an amylin or a peptidic amylin agonist. Liu does not teach administration of an amylin or a peptidic amylin agonist for reducing or moderating a postprandial rise in plasma glucose in a mammal. Since Liu does not teach each and every element of the claim, the reference does not anticipate the claimed invention.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The background section of Meezan discusses that diabetes mellitus is characterized by hyperglycemia and presents as two major subtypes, Type I and Type II. The combination of Liu and Meezan provides no teaching or suggestion of the use of amylin or a peptidic amylin agonist for reducing or moderating a postprandial rise in plasma glucose. Thus, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

In sum, Applicants respectfully submit that the cited references neither anticipate nor make obvious the claimed invention.

Accordingly, Applicants respectfully request reconsideration ad withdrawal of the rejections under 35 U.S.C. §§102(e)/103.

Rejections under Obviousness-type Double Patenting

Claims 24-30 and 38-59 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-35 of U.S. Pat. No. 6,114,304. Claims 24-30, 38, 40-57, and 59 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-18 of U.S. Pat. No. 6,417,164. Although Applicants disagree with these rejections, in order to facilitate prosecution, Applicants are willing to consider submitting a terminal disclaimer in the present application with regard to the cited patents upon indication of allowable subject matter.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the examiner is encouraged to contact Applicants' representative at the Telephone number below.

No further fees are believed due for this submission. However, if a fee is due, the Commissioner is hereby authorized to charge payment of any fees associated with this communication, to Applicant's Deposit Account No. 010535. Additionally, the Commissioner is hereby authorized to charge payment or credit overpayment of any fees during the pendency of this application to Applicant's Deposit Account No. 010535.

Date: 11 October 2005

Respectfully submitted,

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